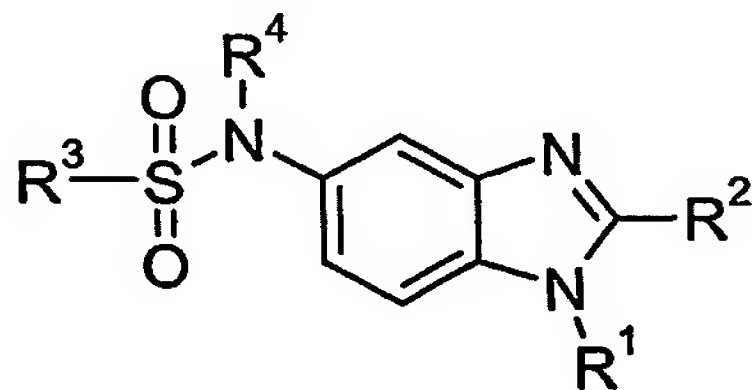


What is claimed is:

1. A compound of Formula I or a pharmaceutically acceptable salt thereof:



I

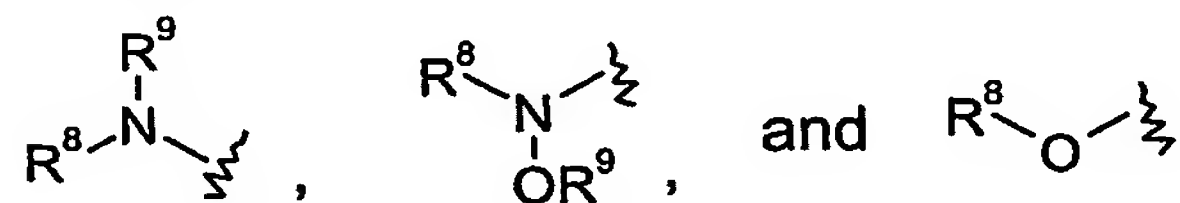
wherein

- R^1 is selected from C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, $R^5R^6N-C_{1-6}$ alkyl, R^5O-C_{1-6} alkyl, $R^5C(=O)N(-R^6)-C_{1-6}$ alkyl, $R^5R^6NS(=O)_2-C_{1-6}$ alkyl, $R^5CS(=O)_2N(-R^6)-C_{1-6}$ alkyl, $R^5R^6NC(=O)N(-R^7)-C_{1-6}$ alkyl, $R^5R^6NS(=O)_2N(R^7)-C_{1-6}$ alkyl, C_{6-10} aryl- C_{1-6} alkyl, C_{6-10} aryl- $C(=O)-C_{1-6}$ alkyl, C_{3-10} cycloalkyl- C_{1-6} alkyl, C_{4-8} cycloalkenyl- C_{1-6} alkyl, C_{3-6} heterocyclyl- C_{1-6} alkyl, C_{3-6} heterocyclyl- $C(=O)-C_{1-6}$ alkyl, C_{1-10} hydrocarbylamino, R^5R^6N- , R^5O- , $R^5C(=O)N(-R^6)-$, $R^5R^6NS(=O)_2-$, $R^5CS(=O)_2N(-R^6)-$, $R^5R^6NC(=O)N(-R^7)-$, $R^5R^6NS(=O)_2N(R^7)-$, C_{6-10} aryl, C_{6-10} aryl- $C(=O)-$, C_{3-10} cycloalkyl, C_{4-8} cycloalkenyl, C_{3-6} heterocyclyl and C_{3-6} heterocyclyl- $C(=O)-$; wherein said C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{6-10} aryl- C_{1-6} alkyl, C_{6-10} aryl- $C(=O)-C_{1-6}$ alkyl, C_{3-10} cycloalkyl- C_{1-6} alkyl, C_{4-8} cycloalkenyl- C_{1-6} alkyl, C_{3-6} heterocyclyl- C_{1-6} alkyl, C_{3-6} heterocyclyl- $C(=O)-C_{1-6}$ alkyl, C_{1-10} hydrocarbylamino, C_{6-10} aryl, C_{6-10} aryl- $C(=O)-$, C_{3-10} cycloalkyl, C_{4-8} cycloalkenyl, C_{3-6} heterocyclyl or C_{3-6} heterocyclyl- $C(=O)-$ used in defining R^1 is optionally substituted by one or more groups selected from halogen, cyano, nitro, methoxy, ethoxy, methyl, ethyl, hydroxy, and $-NR^5R^6$;

- R^2 is selected from C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyl- C_{1-6} alkyl, C_{4-8} cycloalkenyl- C_{1-6} alkyl, C_{3-6} heterocycloalkyl- C_{1-6} alkyl, C_{4-8} cycloalkenyl, R^5R^6N- , C_{3-5} heteroaryl, C_{6-10} aryl and C_{3-6} heterocycloalkyl, wherein said C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl- C_{1-6} alkyl, C_{4-8} cycloalkenyl- C_{1-6} alkyl, C_{3-6} heterocycloalkyl- C_{1-6} alkyl, C_{4-8} cycloalkenyl, C_{3-5} heteroaryl, C_{6-10} aryl or C_{3-6} heterocycloalkyl used in defining R^2 is optionally substituted by one or more groups selected from halogen, cyano, nitro, methoxy, ethoxy, methyl, ethyl, hydroxy, and $-NR^5R^6$;

wherein R^5 , R^6 and R^7 are independently selected from $-H$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, and a divalent C_{1-6} group that together with another divalent R^5 , R^6 or R^7 forms a portion of a ring;

R^3 is selected from $-H$, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyl- C_{1-6} alkyl, C_{4-8} cycloalkenyl- C_{1-6} alkyl, C_{3-6} heterocycloalkyl,



optionally substituted with one or more groups selected from C_{1-6} alkyl, halogen, amino and C_{1-6} alkoxy;

each of R^8 and R^9 is independently selected from $-H$, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyl- C_{1-6} alkyl, C_{3-6} heterocyclyl, C_{6-10} aryl, C_{3-6} heterocyclyl- C_{1-6} alkyl, C_{6-10} aryl- C_{1-6} alkyl, and a divalent C_{1-6} group that together with another divalent group selected from R^8 and R^9 forms a portion of a ring, wherein said C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyl- C_{1-6} alkyl, C_{3-6} heterocyclyl, C_{6-10} aryl, C_{3-6} heterocyclyl- C_{1-6} alkyl, C_{6-10} aryl- C_{1-6} alkyl, or divalent C_{1-6} group is optionally substituted by one or more groups selected from halogen, cyano, nitro, methoxy, ethoxy, methyl, ethyl, hydroxy, and $-NR^5R^6$; and

R^4 is selected from $-H$, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyl- C_{1-6} alkyl, and C_{4-8} cycloalkenyl- C_{1-6} alkyl.

2. A compound as claimed in claim 1, wherein

R^1 is selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, phenyl- C_{1-4} alkyl, C_{3-10} cycloalkyl- C_{1-4} alkyl, C_{4-6} cycloalkenyl- C_{1-4} alkyl, C_{3-10} heterocyclyl- C_{1-4} alkyl, C_{6-10} aryl, C_{3-10} cycloalkyl, C_{3-10} heterocyclyl and C_{4-6} cycloalkenyl, wherein said C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, phenyl- C_{1-4} alkyl, C_{3-10} cycloalkyl- C_{1-4} alkyl, C_{4-6} cycloalkenyl- C_{1-4} alkyl, C_{3-10} heterocyclyl- C_{1-4} alkyl, C_{6-10} aryl, C_{3-10} cycloalkyl, C_{3-10} heterocyclyl and C_{4-6} cycloalkenyl used in defining R^1 is optionally substituted by one or more groups selected from halogen, cyano, nitro, methoxy, ethoxy, methyl, ethyl, hydroxy, and $-NR^5R^6$;

R^2 is selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-4} alkyl, C_{4-6} cycloalkenyl- C_{1-4} alkyl, C_{3-6} heterocycloalkyl- C_{1-4} alkyl, C_{4-6} cycloalkenyl, C_{3-5} heteroaryl, R^5R^6N- , and phenyl, wherein said C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-4} alkyl, C_{4-6} cycloalkenyl- C_{1-4} alkyl,

C₃₋₆heterocycloalkyl-C₁₋₄alkyl, C₄₋₆cycloalkenyl, C₃₋₅heteroaryl, R⁵R⁶N-, and phenyl used in defining R² is optionally substituted by one or more groups selected from halogen, cyano, nitro, methoxy, ethoxy, methyl, ethyl, hydroxy and -NR⁵R⁶;

R³ is selected from -H, C₁₋₆alkyl, C₂₋₆alkenyl, C₃₋₆cycloalkyl, C₃₋

5 C₆heterocycloalkyl, $\text{R}^9-\text{N}(\text{R}^8)_2$ and $\text{R}^8-\text{O}-\text{Z}$ optionally substituted with one or more groups selected from C₁₋₆alkyl and halogen;

each of R⁸ and R⁹ is independently selected from -H, C₁₋₆alkyl, C₂₋₆alkenyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₃₋₆heterocyclyl and C₃₋₆heterocyclyl-C₁₋₆alkyl, wherein said C₁₋₆alkyl, C₂₋₆alkenyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₃₋₆heterocyclyl, C₃₋₆heterocyclyl-C₁₋₆alkyl and a divalent C₁₋₆group that together with another divalent group selected from R⁸ and R⁹ forms a portion of a ring, wherein said C₁₋₆alkyl, C₂₋₆alkenyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₃₋₆heterocyclyl and C₃₋₆heterocyclyl-C₁₋₆alkyl, wherein said C₁₋₆alkyl, C₂₋₆alkenyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₃₋₆heterocyclyl, C₃₋₆heterocyclyl-C₁₋₆alkyl or 15 divalent C₁₋₆group are optionally substituted by one or more groups selected from halogen, cyano, nitro, methoxy, ethoxy, methyl, ethyl, hydroxy and -NR⁵R⁶; and R⁴, R⁵ and R⁶ are independently selected from -H and C₁₋₃alkyl.

3. A compound as claimed claim 1,

20 wherein R¹ is selected from C₁₋₆alkyl, C₂₋₆alkenyl, phenyl-C₁₋₄alkyl, C₃₋₁₀cycloalkyl-C₁₋₄alkyl, C₄₋₆cycloalkenyl-C₁₋₄alkyl, C₆₋₁₀aryl, C₃₋₁₀cycloalkyl, C₃₋₆heterocycloalkyl-C₁₋₄alkyl, and C₄₋₆cycloalkenyl, wherein said C₁₋₆alkyl, C₂₋₆alkenyl, phenyl-C₁₋₄alkyl, C₃₋₁₀cycloalkyl-C₁₋₄alkyl, C₄₋₆cycloalkenyl-C₁₋₄alkyl, C₆₋₁₀aryl, C₃₋₁₀cycloalkyl, C₃₋₆heterocycloalkyl-C₁₋₄alkyl, and C₄₋₆cycloalkenyl used in 25 defining R¹ is optionally substituted by one or more groups selected from halogen, methoxy, ethoxy, methyl, ethyl, hydroxy, and -NR⁵R⁶;

R² is selected from C₁₋₆alkyl, C₂₋₆alkenyl, C₃₋₆cycloalkyl and C₃₋₆cycloalkyl-C₁₋₄alkyl, wherein said C₁₋₆alkyl, C₂₋₆alkenyl, C₃₋₆cycloalkyl and C₃₋₆cycloalkyl-C₁₋₄alkyl used in defining R² is optionally substituted by one or more groups selected 30 from halogen, methoxy, ethoxy, methyl, ethyl, hydroxy and -NR⁵R⁶;

R^3 is selected from C_{2-6} alkyl, C_{3-6} heterocycloalkyl and $R^9-N(R^8)$ optionally substituted with one or more C_{1-6} alkyl, and;

wherein said C_{3-6} heterocycloalkyl contain at least one nitrogen ring atom and the radical of C_{3-6} heterocycloalkyl is located on the at least one nitrogen ring atom, and wherein each of R^8 and R^9 is independently selected from $-H$, C_{1-6} alkyl, morpholinyl- C_{1-3} alkyl, pyrrolidinyl- C_{1-3} alkyl, and piperidinyl- C_{1-3} alkyl, wherein said C_{1-6} alkyl, morpholinyl- C_{1-3} alkyl, pyrrolidinyl- C_{1-3} alkyl, and piperidinyl- C_{1-3} alkyl are optionally substituted by one or more groups selected from halogen, methoxy, ethoxy, methyl, ethyl, hydroxy and $-NR^5R^6$; and

10. R^4 , R^5 and R^6 are independently selected from $-H$ and C_{1-3} alkyl.

4. A compound as claimed in claim 1, wherein

R^1 is selected from cyclohexylmethyl, cyclopentylmethyl, cyclobutylmethyl, cyclopropylmethyl, 4,4-difluorocyclohexanemethyl, cyclohexylethyl, cyclopentylethyl, tetrahydropyranylmethyl, tetrahydrofuranylmethyl, 1-piperidinylethyl, N-methyl-2-piperidinyl-methyl and benzyl;

R^2 is selected from t-butyl, n-butyl, 2-methyl-2-butyl, isopentyl, 2-methoxy-2-propyl, 2-hydroxy-propyl, trifluoromethyl, 1,1-difluoroethyl, 2,2,2-trifluoroethyl, 1-cyclopropyl-ethyl, 1-methyl-propyl, 1,1-dimethyl-propyl, 1,1-dimethyl-3-buten-1-yl, ethyl, and 2-propyl;

R^3 is C_{2-5} alkyl and R^8R^9N- , wherein R^8 and R^9 are independently selected from $-H$, and C_{1-3} alkyl.

5. A compound selected from:

25 *N*-[2-*tert*-Butyl-1-(cyclohexylmethyl)-1*H*-benzimidazol-5-yl]-*N,N,N'*-trimethylsulfamide;

N-[2-*tert*-Butyl-1-(cyclohexylmethyl)-1*H*-benzimidazol-5-yl]-*N',N'*-diethyl-*N*-methylsulfamide;

30

N'-[1-(cyclohexylmethyl)-2-(1,1-dimethylpropyl)-1*H*-benzimidazol-5-yl]-*N,N*-dimethyl-sulfamide;

5 *N*-[2-*tert*-Butyl-1-(tetrahydro-2*H*-pyran-4-ylmethyl)-1*H*-benzimidazol-5-yl]-*N*-methylbutane-1-sulfonamide;

N-[2-*tert*-Butyl-1-(tetrahydro-2*H*-pyran-4-ylmethyl)-1*H*-benzimidazol-5-yl]-*N*-methyl-2-pyrrolidin-1-ylethanesulfonamide;

10 *N*-[2-*tert*-Butyl-1-(tetrahydro-2*H*-pyran-4-ylmethyl)-1*H*-benzimidazol-5-yl]-*N*-methyl-2-morpholin-4-ylethanesulfonamide;

N-[2-*tert*-Butyl-1-(tetrahydro-2*H*-pyran-4-ylmethyl)-1*H*-benzimidazol-5-yl]-*N*-methyl-2-piperidin-1-ylethanesulfonamide;

15 *N*-[2-*tert*-Butyl-1-(tetrahydro-2*H*-pyran-4-ylmethyl)-1*H*-benzimidazol-5-yl]-2-methoxy-*N*-methylethanesulfonamide;

20 *N*-[2-*tert*-Butyl-1-(tetrahydro-2*H*-pyran-4-ylmethyl)-1*H*-benzimidazol-5-yl]-2-[(2-hydroxyethyl)amino]-*N*-methylethanesulfonamide;

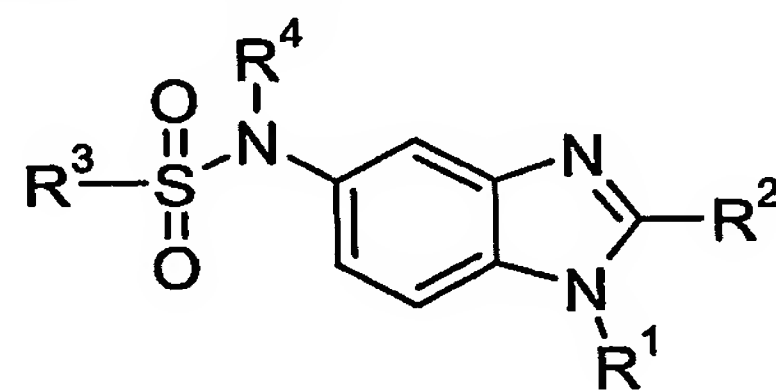
2-(2-Aminoethoxy)-*N*-[2-*tert*-butyl-1-(tetrahydro-2*H*-pyran-4-ylmethyl)-1*H*-benzimidazol-5-yl]-*N*-methylethanesulfonamide;

25 *N*-[2-*tert*-Butyl-1-(tetrahydro-2*H*-pyran-4-ylmethyl)-1*H*-benzimidazol-5-yl]-*N*-methylethanesulfonamide;

N-{2-*tert*-Butyl-1-[(4,4-difluorocyclohexyl)methyl]-1*H*-benzimidazol-5-yl}-*N*-methylbutane-1-sulfonamide;

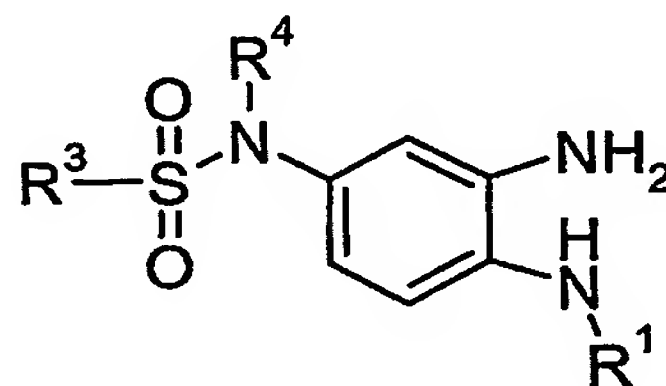
30 *N*-{2-*tert*-Butyl-1-[(4,4-difluorocyclohexyl)methyl]-1*H*-benzimidazol-5-yl}-*N*-methyl-2-piperidin-1-ylethanesulfonamide and pharmaceutically acceptable salts thereof.

6. A compound according to any one of claims 1-5 for use as a medicament.
7. The use of a compound according to any one of claims 1-5 in the manufacture
5 of a medicament for the therapy of pain.
8. The use of a compound according to any one of claims 1-5 in the manufacture
of a medicament for the treatment of anxiety disorders.
- 10 9. The use of a compound according to any one of claims 1-5 in the manufacture
of a medicament for the treatment of cancer, multiple sclerosis, Parkinson's disease,
Huntington's chorea, Alzheimer's disease, gastrointestinal disorders and
cardiovascular disorders.
- 15 10. A pharmaceutical composition comprising a compound according to any one
of claims 1-5 and a pharmaceutically acceptable carrier.
11. A method for the therapy of pain in a warm-blooded animal, comprising the
step of administering to said animal in need of such therapy a therapeutically effective
20 amount of a compound according to any one of claims 1-5.
12. A method for preparing a compound of Formula I,



I

- 25 comprising the step of reacting a compound of Formula II,



II

with a compound of $R^2C(=O)X$, in the presence of a base and optionally a coupling reagent, followed by treatment by an acid;

wherein

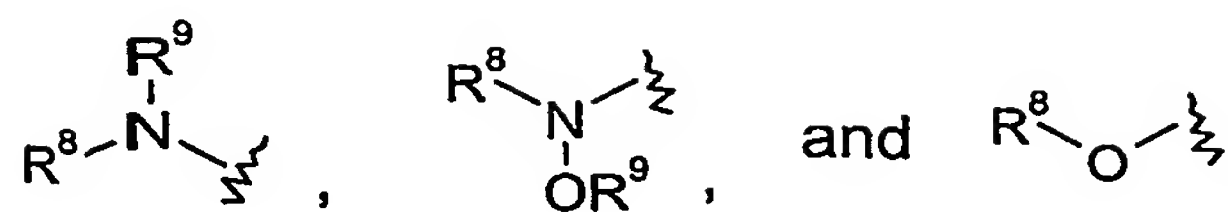
5 X is selected from Cl, Br, F and OH;

R^1 is selected from C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, $R^5R^6N-C_{1-6}$ alkyl, R^5O-C_{1-6} alkyl, $R^5C(=O)N(-R^6)-C_{1-6}$ alkyl, $R^5R^6NS(=O)_2-C_{1-6}$ alkyl, $R^5CS(=O)_2N(-R^6)-C_{1-6}$ alkyl, $R^5R^6NC(=O)N(-R^7)-C_{1-6}$ alkyl, $R^5R^6NS(=O)_2N(R^7)-C_{1-6}$ alkyl, C_{6-10} aryl- C_{1-6} alkyl, C_{6-10} aryl- $C(=O)-C_{1-6}$ alkyl, C_{3-10} cycloalkyl- C_{1-6} alkyl, C_{4-8} cycloalkenyl- C_{1-6} alkyl, C_{3-6} heterocyclyl- C_{1-6} alkyl, C_{3-6} heterocyclyl- $C(=O)-C_{1-6}$ alkyl, C_{1-10} hydrocarbylamino, R^5R^6N- , R^5O- , $R^5C(=O)N(-R^6)-$, $R^5R^6NS(=O)_2-$, $R^5CS(=O)_2N(-R^6)-$, $R^5R^6NC(=O)N(-R^7)-$, $R^5R^6NS(=O)_2N(R^7)-$, C_{6-10} aryl, C_{6-10} aryl- $C(=O)-$, C_{3-10} cycloalkyl, C_{4-8} cycloalkenyl, C_{3-6} heterocyclyl and C_{3-6} heterocyclyl- $C(=O)-$; wherein said C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{6-10} aryl- C_{1-6} alkyl, C_{6-10} aryl- $C(=O)-C_{1-6}$ alkyl, C_{3-10} cycloalkyl- C_{1-6} alkyl, C_{4-8} cycloalkenyl- C_{1-6} alkyl, C_{3-6} heterocyclyl- C_{1-6} alkyl, C_{3-6} heterocyclyl- $C(=O)-C_{1-6}$ alkyl, C_{1-10} hydrocarbylamino, C_{6-10} aryl, C_{6-10} aryl- $C(=O)-$, C_{3-10} cycloalkyl, C_{4-8} cycloalkenyl, C_{3-6} heterocyclyl or C_{3-6} heterocyclyl- $C(=O)-$ used in defining R^1 is optionally substituted by one or more groups selected from halogen, cyano, nitro, methoxy, ethoxy, methyl, ethyl, hydroxy, and $-NR^5R^6$;

R^2 is selected from C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyl- C_{1-6} alkyl, C_{4-8} cycloalkenyl- C_{1-6} alkyl, C_{3-6} heterocycloalkyl- C_{1-6} alkyl, C_{4-8} cycloalkenyl, R^5R^6N- , C_{3-5} heteroaryl, C_{6-10} aryl and C_{3-6} heterocycloalkyl, wherein said C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl- C_{1-6} alkyl, C_{4-8} cycloalkenyl- C_{1-6} alkyl, C_{3-6} heterocycloalkyl- C_{1-6} alkyl, C_{4-8} cycloalkenyl, C_{3-5} heteroaryl, C_{6-10} aryl or C_{3-6} heterocycloalkyl used in defining R^2 is optionally substituted by one or more groups selected from halogen, cyano, nitro, methoxy, ethoxy, methyl, ethyl, hydroxy, and $-NR^5R^6$;

wherein R^5 , R^6 and R^7 are independently selected from $-H$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, and a divalent C_{1-6} group that together with another divalent R^5 , R^6 or R^7 forms a portion of a ring;

R^3 is selected from $-H$, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyl- C_{1-6} alkyl, C_{4-8} cycloalkenyl- C_{1-6} alkyl, C_{3-6} heterocycloalkyl,



optionally substituted with one or more

groups selected from C₁₋₆alkyl, halogen, amino and C₁₋₆alkoxy;

each of R⁸ and R⁹ is independently selected from -H, C₁₋₁₀alkyl, C₂₋₁₀alkenyl, C₂₋₁₀alkynyl, C₃₋₁₀cycloalkyl, C₃₋₁₀cycloalkyl-C₁₋₆alkyl, C₃₋₆heterocyclyl, C₆₋₁₀aryl, C₃₋₆heterocyclyl-C₁₋₆alkyl, C₆₋₁₀aryl-C₁₋₆alkyl, and a divalent C₁₋₆group that together with another divalent group selected from R⁸ and R⁹ forms a portion of a ring, wherein said C₁₋₁₀alkyl, C₂₋₁₀alkenyl, C₂₋₁₀alkynyl, C₃₋₁₀cycloalkyl, C₃₋₁₀cycloalkyl-C₁₋₆alkyl, C₃₋₆heterocyclyl, C₆₋₁₀aryl, C₃₋₆heterocyclyl-C₁₋₆alkyl, C₆₋₁₀aryl-C₁₋₆alkyl, or divalent C₁₋₆group is optionally substituted by one or more groups selected from halogen, cyano, nitro, methoxy, ethoxy, methyl, ethyl, hydroxy, and -NR⁵R⁶; and

R⁴ is selected from -H, C₁₋₁₀alkyl, C₂₋₁₀alkenyl, C₂₋₁₀alkynyl, C₃₋₁₀cycloalkyl, C₃₋₁₀cycloalkyl-C₁₋₆alkyl, and C₄₋₈cycloalkenyl-C₁₋₆alkyl.